04.28.05

AF/T647

TRANSMITTAL OF APPEAL BRIEF

Docket No. 01017/39996

In re Application of: John E. Sims

Application No.	Filing Date	Examiner	Group Art Unit
09/598,443-Conf. #5571	June 22, 2000	F. M. Hamud	1647

Invention: SIGIRR DNA AND POLYPEPTIDES

TO THE COMMISSIONER OF PATENTS:

Transmitted herewith is the Appeal Brief in this application, with respect to the Notice of Appeal filed: December 27, 2004 .

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William K. Merkel Dated: April 27, 2005

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Richard Zimmermann

Docket No.: 01017/39996
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re Patent Application of:
John E. Sims

Application No.: 09/598,443 Confirmation No.: 5571

Filed: June 22, 2000 Art Unit: 1647

For: SIGIRR DNA AND POLYPEPTIDES Examiner: Fozia M. Hamud

APPEAL BRIEF

MS Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

This brief is timely filed under 37 C.F.R. § 41.37(a) and is filed in support of the appeal.

The fees required under 37 C.F.R. § 41.20(b)(2) are addressed in the accompanying TRANSMITTAL OF APPEAL BRIEF.

This brief contains items under the following headings as required by 37 C.F.R. § 41.37 and M.P.E.P. § 1206:

I.	Real Party In Interest
II	Related Appeals and Interferences
III.	Status of Claims
IV.	Status of Amendments
V.	Summary of Claimed Subject Matter
VI.	Grounds of Rejection to be Reviewed on Appeal
VII.	Argument
VIII.	Claims
IX.	Evidence
X.	Related Proceedings
Claims Appendix	Claims

I. REAL PARTY IN INTEREST

Immunex Corporation is the assignee of the above-captioned application, as evidenced by an assignment of the entire right, title and interest in the application recorded in the U.S. Patent and Trademark Office at reel 011172, frame 0558. In 2002, Immunex Corporation was acquired by Amgen Inc. As such, the real party in interest for this appeal is:

AMGEN INC.

II. RELATED APPEALS, INTERFERENCES, AND JUDICIAL PROCEEDINGS

There are no related appeals, interferences, or judicial proceedings.

III. STATUS OF CLAIMS

A. Total Number of Claims in Application

There are a total of 27 claims pending in the application. The pending claims are claims 34-60, attached hereto in a Claims Appendix. Claims 1-33 were canceled during prosecution. Each one of pending claims 34-60 has been twice rejected. Collectively, the rejected claims 34-60 form the subject of this appeal.

B. Current Status of Claims

1. Claims canceled: 1-33.

2. Claims withdrawn from consideration but not canceled: none.

3. Claims pending: 34-60.

4. Claims allowed: none.

5. Claims rejected: 34-60.

C. Claims On Appeal

The claims on appeal are claims 34-60.

IV. STATUS OF AMENDMENTS

An Amendment Pursuant to 37 C.F.R. § 1.116 was filed on April 26, 2005. Applicant has not been informed of the status of that amendment and, on that basis, identifies the status of the amendment as non-entered.

V. SUMMARY OF CLAIMED SUBJECT MATTER

The claims of the present invention are directed to compositions that comprise a nucleic acid comprising a sequence that encodes a SIGIRR (Single Immunoglobulin domain-containing Interleukin-1 Receptor-related) polypeptide and methods of using such nucleic acid compositions to produce SIGIRR polypeptides by recombinant expression.

VI. GROUNDS OF OBJECTION TO BE REVIEWED ON APPEAL

The issues presented on appeal are as follows:

1. Did the Examiner fail to establish a *prima facie* basis for lack of patentable utility?

2. Did the Examiner specifically fail to show that one of ordinary skill in the art would be more likely than not to doubt or question the truth of the assertion in the specification that the claimed nucleic acids were useful in identifying the 11p15.5 chromosomal locus expressly disclosed in the specification to be associated with the phenomenon of loss of heterozygosity (LOH) involved in a variety of medically recognized diseases (e.g., Wilm's tumor (type 2))?

3. Did the Examiner specifically fail to show that one of ordinary skill in the art would be more likely than not to doubt or question the truth of the assertion in the specification that the claimed SIGIRR (Single Immunoglobulin domain-containing Interleukin-1 Receptor-related) molecules contribute to the binding of IL-1?

4. Did the Examiner err in failing to establish lack of an asserted patentable use as a basis for rejecting claims 34-60 for lack of enablement when the reasoning underlying the rejection was the impossibility of teaching a use for subject matter lacking an asserted patentable utility?

5. Did the Examiner err in rejecting claims 59 and 60 for indefiniteness based on the unsubstantiated possibility that more than one type of

nucleic acid (or polypeptide) would share the abbreviation "TIGIRR" and meet the additional limitations of either of those claims?

VII. ARGUMENT

A. The Claimed Subject Matter is Supported by an Assertion of Patentable Utility.

Section 101 of Title 35, United States Code, imposes a statutory requirement for patentable utility to obtain a U.S. patent. As construed by the courts and as understood by the Commissioner for Patents, a patentable utility must either be asserted in the application or must be well-established in the art as of the effective filing date. To satisfy the statutory requirement, a patentable utility must be a specific, substantial and credible utility of the claimed subject matter. A specific utility in the context of compositions, the subject matters of claims 34-58, is any substantial utility that is not shared by all members of the relevant class of compositions. In requiring a specific utility, the statute eliminates "throw away" or trivial utilities such as the use of isolated nucleic acids as molecular weight markers or as landfill. A substantial utility is a real-world utility, i.e., a utility in a form that is presently realizable as opposed to, e.g., the subject of further research to identify a therapeutically useful molecule. A credible utility is a utility that, on a preponderance of all of the evidence of record, would not lead one of skill in the art to be more likely than not to question, or doubt, the asserted utility.

In assessing whether an application satisfies the requirement for patentable utility, the courts have established that the United States Patent and Trademark Office (the patent office) bears the initial burden of presenting a *prima facie* case of lack of patentable utility. *In re Oetiker*, 977 F. 2d 1443, 1445, 24 U.S.P.Q. 2d 1443, 1444 (Fed. Cir. 1992). The *prima facie* showing must be set forth in a well-reasoned statement supported by documentary evidence or specific explanations of the scientific basis for the factual conclusion. *Id.*, *see also* M.P.E.P. § 2107.02 (IV). Further, the patent office must provide a sufficient evidentiary basis for any factual assumptions relied upon in making the showing. *In re Gaubert*, 524 F. 2d 1222, 1224, 187 U.S.P.Q. 664, 666 (C.C.P.A. 1975). Moreover where, as here, an assertion of patentable utility is provided in an application, that assertion is accorded a presumption of utility. *See In re Jolles*, 628 F. 2d 1322, 206 U.S.P.Q. 885

(C.C.P.A. 1980), *In re Langer*, 503 F. 2d 1380, 183 U.S.P.Q. 288 (C.C.P.A. 1974). Consistent with the presumption is the following instruction from *Langer*.

> As a matter of Patent Office practice, a specification which contains a disclosure of utility which corresponds in scope to the subject matter sought to be patented must be taken as sufficient to satisfy the utility requirement of § 101 for the entire claimed subject matter unless there is a reason for one skilled in the art to question the objective truth of the statement of utility or its scope.
>
> *Langer*, 503 F. 2d at 1391, 183 U.S.P.Q. at 297 (emphases in original).

To overcome the presumption of utility and establish that an application fails to satisfy the requirement for patentable utility, the patent office must show, by a preponderance of the evidence of record, that it is more likely than not that one of ordinary skill in the art would doubt (i.e., "question") the truth of the statement of utility, a question of fact. *See Raytheon v. Roper*, 724 F. 2d 951, 956, 220 U.S.P.Q. 592, 596 (Fed. Cir. 1983) *cert. denied* 469 U.S. 835 (1984); *see also* M.P.E.P. § 2107.02 (III) (A).

Application of the law of patentable utility to the instant facts involves a consideration of claims 34-58, which are drawn to isolated nucleic acid molecules that include Single Ig domain-containing Interleukin-1 Receptor-Related (i.e., SIGIRR) molecules, as well as derivative compositions such as vectors comprising such molecules and host cells comprising such vectors. Claims 59 and 60 are drawn to methods for producing TIGIRR polypeptides from host cells (TIGIRR polypeptides and SIGIRR polypeptides are not mutually exclusive polypeptide groups insofar as these groups include related receptors).

In view of the claimed subject matter, Applicants have noted on the record that two assertions of patentable utility are provided in the application as filed. First, the application discloses that the claim-recited nucleic acid molecules map to a particular site, or chromosomal locus, that is subject to genetic rearrangements (e.g., rearrangements resulting in loss of heterozygosity or LOH), with these genetic rearrangements being associated with a number of diseases, such as Wilm's tumor (type 2). *See* specification, page 10, lines 10-18 and page 37, line 27 to page 38, line 7. (For a discussion of LOH, *see* Deng et al., Science 274:2057-2059 (1996), made of record by citation on a Form PTO-1449 filed with Applicants' amendment of May 27, 2003; "heterozygosity" has a well-known meaning in the

art, as illustrated in Strickberger et al., Genetics, 2d Ed., p. 117 (MacMillan Publishing Co., Inc., New York, 1976), attached as Appendix A to the Amendment Pursuant to 37 C.F.R. § 1.116 filed April 26, 2005.) Second, the application discloses that the claimed nucleic acid molecules contribute to the modulation of Interleukin-1-mediated inflammatory and immunological processes. *See* specification, page 42, line 26 to page 43, line 7. Each of these assertions of patentable utility is commensurate in scope to the claimed subject matter and either assertion alone satisfies the requirement for patentable utility under 35 U.S.C. § 101.

1. The claimed subject matter is patentably useful as a disease marker.

The first assertion of patentable utility identified above, that the nucleic acid molecules and derivative compositions of the claims are useful in diagnosing a number of diseases, is based on the application's disclosure of the following facts. First, SIGIRR nucleic acid maps to chromosome locus 11p15.5. Second, chromosome locus 11p15.5 is involved in genetic rearrangements such as the loss of heterozygosity (LOH). And third, LOH at chromosome locus 11p15.5 is associated with the diseases (e.g., Wilm's tumor (type 2)) expressly identified at page 10, lines 13-18, of the application as filed.

This assertion of utility identifies a specific utility of the subject matter of claims 34-60. The utility is specific to particular nucleic acid molecules that map to chromosome locus 11p15.5. The utility is also specific to particular diseases associated with genetic rearrangements at chromosome locus 11p15.5 that would be amenable to prognosis and/or diagnosis using the claimed nucleic acid molecules as markers.

The assertion that the claimed subject matter is useful as a disease marker is also an assertion of a substantial, or "real world," utility in that the marker molecules are presently available for use in diagnosing real-world instances of the specifically identified diseases. This assertion of utility is therefore not an assertion of (a) basic research designed to identify properties or mechanisms of action of the claimed molecules, (b) methods of treating unspecified diseases, (c) methods of assaying for materials that themselves have no substantial utility, or (d) methods of making materials having no substantial utility, the examples of insubstantial utilities provided in the patent office's Revised Utility Examination Guidelines, Fed. Reg. 66:1092 (January 5, 2001) at page 6 (Utility Guidelines).

One of skill in the art would recognize that a nucleic acid molecule mapping to chromosome locus 11p15.5 would be useful in detecting a genetic rearrangement, such as the LOH associated with the identified diseases, in a given sample because an LOH would affect the complexity of a hybridization pattern resulting from hybridizing a target (i.e., genomic SIGIRR sequences) to a marker molecule of the invention. One of skill in the art would recognize that loss of heterozygosity in a diploid organism (e.g., man), for example, would result in loss of one of the two distinct (i.e., non-duplicative) copies of chromosomal locus 11p15.5. Stated alternatively, the skilled person would recognize that one of the two dissimilar alleles of SIGIRR would be lost in LOH individuals. Upon fragmentation of the genomic DNA in the course of performing standard hybridization reactions with a marker molecule of the invention, the person of ordinary skill in the art would have understood that the pattern of hybridized fragments would be less complex than the pattern resulting from a like-situated individual that did not suffer LOH. The difference in hybridization patterns provide a basis for assessing genetic rearrangements at locus 11p15.5, thereby providing a basis for using the claimed subject matter in the specific, real-world prognosis and/or diagnosis of expressly identified diseases associated with genetic rearrangements at this chromosomal locus. Thus, the assertion of a utility for the claimed nucleic acid molecules as being useful in the prognosis and/or diagnosis of specific diseases associated with genetic rearrangements such as LOH at the chromosome 11p15.5 locus is an assertion of a specific and substantial utility in the application as filed.

The foregoing argument establishing that use of the claimed nucleic acid molecules as markers for diseases associated with genetic rearrangements at chromosome locus 11p15.5 was made of record in Applicants' amendment of May 27, 2003. In response, the Examiner found the argument unpersuasive and provided the following remarks in support:

> the fact that the claimed nucleic acid sequence has been mapped to chromosome 11p15.5 region, does not provide utility for the claimed nucleic acid. There is no doubt that that chromosome 11p15.5 is associated with loss of heterozygosity (LOH), in a number of diseases including Wilm's tumor, rhahbdomyoscarcoma, breast cancer, non-small cell lung carcinoma (NSCLC), however, the role of the claimed nucleic acid in any of these diseases is not disclosed by Applicants. The claimed nucleic acid can't be used to diagnose any

> disorder, because instant specification does not establish a link between the claimed nucleic acid and any disorder. High incidence of LOH might be observed in certain tumors, however, the specific role of the genes mapped on a locus of a chromosome associated with LOH must be delineated. For example, is there a reduction or over-production of said gene relative to control tissues? Instant specification does not demonstrate whether the claimed nucleic acid itself is involved in the recited diseases or whether it is the encoded protein. Is it the over-expression or under-expression of the claimed nucleic acid itself that is associated with these diseases? No meaningful information will be obtained from tracking the level of expression of the claimed nucleotide or mapping the locus on a chromosome in which the claimed DNA is located, because there is no physiological or biological significance attached to these nucleotides or the encoded proteins.
>
> Office Action mailed August 12, 2003 at pages 3-4.

Applicants note the patent office's acknowledgement of the following facts: (1) the claimed nucleic acid molecules map to chromosome 11p15.5 ("the fact that the claimed nucleic acid sequence has been mapped to chromosome 11p15.5 region"), (2) the chromosome 11p15.5 locus is associated with LOH ("[t]here is no doubt that that chromosome 11p15.5 is associated with loss of heterozygosity (LOH), in a number of diseases including Wilm's tumor, rhahbdomyoscarcoma, breast cancer, non-small cell lung carcinoma . . . ."), and (3) LOH is associated with a number of real-world diseases (*Id.*). The remainder of the patent office's position is devoted to establishing that the application did not disclose the specific role of the claimed nucleic acids in any of the specified diseases, a point that need not be reached because it is irrelevant to the issue of patentable utility based on use of the claimed subject matter as a marker for the disease states.

One of skill in the art would readily recognize that LOH in a particular region of a genome would result in reduced complexity when mapping that region. A well-established fundamental principle of genetics is that a diploid cell that is heterozygous for a given gene means that the two alleles of that gene are different. Thus, when mapped by fragmenting the genome and hybridizing a marker or probe to the fragmented genome, two different patterns of fragments (one for each allele) will be effectively combined and detected, leading to a complex hybridization pattern. Loss of heterozygosity in such a cell would result in a loss of one of the two patterns of fragments. That loss would be revealed by a reduction in the complexity of the pattern of hybridizing fragments. When loss of one of

the two patterns is associated with a disease, as in the present case, the marker or probe is useful in the prognosis or diagnosis of the associated disease state. It is apparent that the physiological role of the marker or probe nucleic acid, or the role of any encoded polypeptide, is irrelevant to the use of a nucleic acid as a marker in the prognosis or diagnosis of disease.

The foregoing discussion establishes that the patent office and Applicants agree on the facts relevant to an assertion of patentable utility in the form of a nucleic acid marker or probe for diseases associated with genetic rearrangements at chromosome locus 11p15.5. The patent office and Applicants agree that the claimed nucleic acid molecules map to chromosome locus 11p15.5 and both parties agree that known diseases are associated with genetic rearrangements at that chromosomal locus, including LOH. Therefore, there is no reasonable basis for questioning this assertion of patentable utility. *See Cross v. Iizuka*, 753 F. 2d 1040, 224 U.S.P.Q. 739 (Fed. Cir. 1985) (an assertion of utility is credible unless it is merely a generalized nebulous expression such as "biological properties"); *see also Nelson v. Bowler*, 626 F. 2d 853, 856, 206 U.S.P.Q. 881, 883 (C.C.P.A. 1980). The patent office, unable to provide a reasonable basis for questioning Applicants' assertion of patentable utility, has been unable to overcome the presumption of utility attaching to Applicants' assertion. Accordingly, the patent office has failed to establish a *prima facie* basis for lack of patentable utility.

The *prima facie* showing of lack of patentable utility must be set forth in a well-reasoned statement supported by documentary evidence or specific explanations of the scientific basis for the factual conclusion (*see* M.P.E.P. § 2107.02 (IV)), and this has not been provided in the present record. Moreover, based on Applicants' reasoning provided above, it is submitted that the patent office cannot provide a well-reasoned statement, supported by evidence or explanation, questioning the asserted utility of the claimed nucleic acid molecules as markers for diseases associated with genetic rearrangements at chromosome locus 11p15.5.

The foregoing assertion of patentable utility in the form of a marker for specific diseases is commensurate in scope to the claims at issue in this appeal. In view of the requirement to provide a single patentable utility for the subject matter of a pending

claim, Applicants submit that the preceding argument alone is sufficient to establish patentable utility for the subject matters of claims 34-60. *See Raytheon*, 724 F. 2d at 958, 220 U.S.P.Q. at 598 ("When a properly claimed invention meets at least one stated objective, utility under 35 U.S.C. 101 is clearly shown."); *In re Gottlieb*, 328 F. 2d 1016, 1019, 140 U.S.P.Q. 665, 668 (C.C.P.A. 1964) ("Having found that the [product] is useful for some purpose, it becomes unnecessary to decide whether it is in fact useful for the other purposes 'indicated' in the specification as possibly useful.") The rejection of claims 34-60 under 35 U.S.C. § 101 should be reversed.

2. *The claimed subject matter is patentably useful in modulating IL-1-mediated inflammation and immune responses.*

The second assertion of patentable utility identified above, that the claimed nucleic acid molecules modulate IL-1-mediated inflammatory and/or immune responses, is implied by the name of the claimed molecules – SIGIRR, or single Immunoglobulin domain-containing IL-1 Receptor-Related, molecules (including TIGIRR, or three-Immunoglobulin domain-containing IL-1 Receptor-Related, molecules). One of skill in the art would understand that a molecule known as an IL-1 receptor-related molecule would encode a polypeptide that participated in IL-1 binding. Further, the skilled person would immediately recognize that the binding of IL-1 would sequester at least some biologically active IL-1, thereby affecting or modulating the inflammatory and/or immune responses dependent upon, or influenced by, IL-1 activity. *See* specification, page 1, line 14 to page 3, line 25.

Applicants corroborated the truth of this assertion in the application as filed by adding post-filed references to the record (*see* Amendment of July 19, 2004, Appendixes B-E). For example, Wald et al., Nature Immunol. 4:920-927 (2003) confirms that SIGIRR is an IL-1 receptor family member (*see* abstract), while O'Neill, Nature Immunol. 4:823-824 (2003), Mantovani et al., J. Leukoc. Biol. 75:738 (2004) (abstract), and Polentarutti et al., Eur. Cytokine Netw. 14:211 (2003) (abstract) all confirm that SIGIRR is a decoy receptor that negatively regulates IL-1 activity. Each of these post-filed publications confirms Applicants' assertion in the application as filed that SIGIRR is a member of the IL-1 Receptor family (*see* specification, page 9, lines 27-28), consistent with the name of the molecule. The Examiner misconstrued the purpose of providing such references in arguing that post-filed documents cannot be used to establish an assertion of patentable utility. Office

Action mailed August 24, 2004 at pages 7-8. Applicants have relied on these post-filed references to corroborate, or confirm, the assertions of patentable utility provided in the application as filed.

The assertion that the claimed nucleic acid molecules would encode polypeptides that modulate IL-1-mediated inflammatory and/or immune responses is a credible assertion of a specific and substantial utility. The asserted utility is specific to those molecules encoding polypeptides actively contributing to the binding of IL-1, and not generally applicable to all nucleic acids or even to all polypeptide-encoding nucleic acids. Thus, the asserted utility is not the type of general utility characteristic of the "throw-away" utilities applicable to an entire class of molecules, i.e., non-specific utilities that are not patentable utilities.

The asserted utility is also a substantial utility in that it is available in presently realizable form and would be beneficial in modulating IL-1 activity in inflammatory and/or immunological responses mediated by IL-1. The central involvement of IL-1, an inflammatory/immunological cytokine, in the processes of inflammation and immunological responses was well known in the art as of the effective filing date of the instant application, and the patent office has not challenged that fact. (*See, e.g.,* Rhezzi et al., Ann. First Super. Sanita 26:263-272 (1990), attached as Appendix B to Applicants' Amendment Pursuant to 37 C.F.R. § 1.116 filed April 26, 2005.) One of skill in the art would immediately recognize that any molecule, including the polypeptides encoded by the claim-recited nucleic acid molecules, that is capable of participating in the binding of IL-1 would be useful in modulating inflammatory and/or immunological responses mediated by IL-1. The application as filed discloses the claim-recited molecules as useful in compositions for modulating these "real world" inflammatory and immunological conditions; the application does not disclose the claim-recited molecules as mere objects of research interest that, with additional analysis, may some day lead to an understanding of their practical utility (i.e., insubstantial and, thus, non-patentable utilities). Accordingly, the assertion of using the claim-recited molecules to modulate IL-1-mediated inflammatory and/or immunological responses in the application as filed is an assertion of a substantial utility.

The foregoing argument establishes that the assertion that the claimed molecules were useful in modulating IL-1-mediated inflammatory and/or immunological responses is an assertion of a specific and substantial utility for that subject matter. The assertion of that utility is also credible. Under the law, that assertion is entitled to a presumption of utility and the patent office has the burden of overcoming that presumption by providing a well-reasoned statement, supported by evidence and/or explanation, that establishes by a preponderance of all of the evidence of record that one of skill in the art would be more likely than not to question or doubt that the claim-recited IL-1 receptor-related molecules would participate in the binding, and thereby affect or modulate the available activity, of IL-1. The patent office has not carried that burden.

Although the Examiner acknowledged that the application as filed contained a disclosure that SIGIRR "may serve as a third component of a signaling complex with IL-R and IL-1R AcP" (*see* Office Action mailed November 26, 2002 at page 3), the Examiner also noted that the application stated that "the N-terminal domain is predicted to function poorly as a signal peptide" and that "the extracellular domain of SIGIRR polypeptide is unlikely to bind an IL-1 family ligand." *Id.* The Examiner repeated the observation regarding the functioning of the N-terminal domain of SIGIRR as a signal peptide and noted that the application did not disclose the identification of any ligand bound by SIGIRR. *See* Office Action mailed August 24, 2004, at page 3. Whether the N-terminal domain of SIGIRR functions poorly or not as a signal peptide is not probative on the issue of whether the claimed SIGIRR molecules were asserted to have a patentable utility. The absence of a signal peptide to facilitate secretion would lead one of skill to expect a receptor-related molecule to be found either intracellularly or in the cell membrane. The application disclosed that SIGIRR was found in the membrane. *See* specification, page 9, lines 24-25. Thus, the relatively "poor" function (not an asserted absence of function) of the N-terminal domain as a signal peptide is of no moment in assessing patentable utility. The application does state that "the extracellular portion of SIGIRR polypeptide is unlikely to bind an IL-1 family ligand since it has a single Ig domain," but that very sentence also states that SIGIRR may "serve as a third component of a signaling complex with IL-1R and IL-1R AcP. . . ." *See* specification, page 9, lines 26-28. One of skill in the art would expect a "third component" of an IL-1 binding complex to participate in the binding of IL-1, thereby contributing to the modulation

of IL-1 activity. This assertion, found in the application as filed, is corroborated by the post-filed references addressed above, all of which provide disclosures consistent with Applicants' assertion in the application as filed. This assertion that SIGIRR participates in IL-1 binding, thereby contributing to the modulation of IL-1 activity in inflammatory and immune responses, is a credible assertion of a specific and substantial utility.

Example 10 of the Utility Guidelines, upon which Applicants continue to rely, provides a set of facts analogous to the instant facts. In Example 10 of those Guidelines, patentable utility was demonstrated for a nucleic acid of disclosed sequence that showed homology to a class of polynucleotides encoding DNA ligases. Because the DNA ligases had a known use in ligating DNA, claims to a nucleic acid of disclosed sequence and identified relationship to DNA ligases were supported by an assertion of patentable utility. In like manner, the present claims are drawn to nucleic acids of disclosed sequences that encode polypeptides that are identified as IL-1 receptor-related molecules by sequence comparisons. One of skill in the art would reasonably expect an IL-1 receptor-related molecule to participate in the binding of IL-1, just as one of skill would expect a DNA ligase to ligate DNA. For DNA ligases, that expectation is not undercut by the known sequence variations of DNA ligases, nor by the known differences in the ligation reactions being catalyzed. For example, prokaryotic DNA ligases, typified by *Escherichia coli* DNA ligase, use nicotine adenine dinucleotide as an energy source for the ligation reaction while eukaryotic and viral DNA ligases, exemplified by T4 DNA ligase, use rATP as an energy source. *See* New England Biolabs catalog, 1996-97 at pages 82-85, attached as Appendix C to the Amendment Pursuant to 37 C.F.R. § 1.116 filed April 26, 2005. Both groups of DNA ligases catalyze the formation of a covalent phosphodiester linkage between DNA molecules, but T4 DNA ligases will also catalyze ligation of RNA molecules. Notwithstanding these differences, the patent office's Utility Guidelines instruct that sequence similarity to a DNA ligase is sufficient to satisfy the requirement for patentable utility. For IL-1 receptor-related molecules, a number of ligands may be identified with the IL-1 superfamily and particular receptors may bind one or another of these ligands, but each of the IL-1 receptor-related molecules participates in the transmission of IL-1 signal, much like all DNA ligases participate in the formation of DNA phosphodiester linkages. Thus, Example 10 of the Utility Guidelines supports Applicants' position that the instant application provides an

assertion of patentable utility in the form of an assertion that SIGIRR molecules contribute to the binding of IL-1 and thereby affect or modulate Il-1-mediated inflammatory and immune responses.

For all of the foregoing reasons, Applicants submit that the rejection of claims 34-60 under 35 U.S.C. § 101 was in error. Accordingly, Applicants request that the rejection be reversed.

B. The Claimed Subject Matter is Enabled

The sole basis for rejecting claims 34-60 under 35 U.S.C. § 112, first paragraph, for lack of enablement is the asserted lack of patentable utility. The implicit reasoning in support of the rejection is that an application cannot teach how to use that which lacks a patentable use. Thus, the instant rejection of the claims stands or falls with the rejection of claims 34-60 under 35 U.S.C. § 101 for lack of patentable utility. As established above, however, the claimed subject matter is supported by at least two assertions of patentable utility in the application as filed. The Examiner's position, therefore, is based on a flawed premise and, for that reason, the instant claim rejection is unsupported. The Examiner has not established a *prima facie* basis for lack of enablement of the subject matter of any of claims 34-60 under 35 U.S.C. § 112, first paragraph, for lack of enablement and the rejection should be reversed.

C. Claims 59 and 60 Are Definite Under 35 U.S.C. § 112, Second Paragraph.

The Amendment Pursuant to 37 C.F.R. § 1.116 filed April 26, 2005, requested that the Examiner exercise discretion in favor of entering the amendment, which effectively clarifies the nature of the subject matter of claims 59 and 60 without altering the scope of either claim. Upon entry of that amendment, Applicants submit that the rejection of claims 59 and 60 under 35 U.S.C. § 112, second paragraph, will have been rendered moot and may properly be withdrawn. Applicants have not received notification of the entry of that amendment and withdrawal of the rejection under § 112, second paragraph. Accordingly, Applicants provide the following argument contingent upon non-entry of the amendment and maintenance of the rejection of claims 59 and 60 under § 112, second paragraph, for indefiniteness.

In the Office Action mailed August 24, 2004, the Examiner maintained the rejection of claims 59 and 60 for asserted indefiniteness in effectively reciting the term "TIGIRR." In support, the Examiner asserted that the term "TIGIRR" is an acronym and it is unclear what the acronym stands for, with several polypeptides possibly being known by that acronym. *See* Office Action at page 9. In response, Applicants' maintain that "TIGIRR" is an abbreviation of the well-known term "Three Immunoglobulin domain-containing Interleukin-1 Receptor-Related." The Examiner has not identified a second term that would be abbreviated "TIGIRR" and, therefore, whether the name is fully spelled out or abbreviated is irrelevant to the issue of definiteness. Either "TIGIRR" and "Three Immunoglobulin-containing Interleukin-1 Receptor-Related" are definite in unambiguously referring to particular subject matter, or they both are indefinite. To maintain that there is a mere possibility that another term would share the "TIGIRR" abbreviation is to deny Applicant the opportunity to serve as its own lexicographer and does not comply with 35 U.S.C. § 112, second paragraph. The Examiner has failed to identify any other term sharing the "TIGIRR" abbreviation and there is, therefore, no reasonable basis for confusion in recitation of that term in the presently pending claims. Thus, the Examiner has erred in failing to establish a *prima facie* basis for rejecting either of claims 59 and 60 under § 112, second paragraph, for alleged indefiniteness in the recitation of "TIGIRR."

Beyond the preceding dispositive reason for reversing the rejection, Applicants note that the term "TIGIRR" is not recited in isolation in the rejected claims. The subject matter of each of those claims is defined in unambiguous structural and functional terms. The Examiner has not provided any possible molecule identified by a term that is or may be abbreviated "TIGIRR" and that shares the structural and functional limitations of either of pending claims 59 or 60. Accordingly, the Examiner has failed to establish a *prima facie* basis for rejecting claims 59 and 60 under 35 U.S.C. § 112, second paragraph, and the rejection should be reversed.

VIII. CLAIMS

A copy of the claims involved in the present appeal as they presently appear in the record is attached hereto as the "Claims Appendix." Also provided in the "Claims

Appendix" is a copy of the pending claims as they would appear upon entry of the Amendment filed April 26, 2005.

IX. EVIDENCE

No evidence pursuant to 37 C.F.R. §§ 1.130, 1.131, or 1.132 or entered by or relied upon by the examiner is being submitted.

X. RELATED PROCEEDINGS

There are no related proceedings and, hence, no appendix is included.

Dated: April 27, 2005

Respectfully submitted,

By 

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CLAIMS APPENDIX

Claims Involved in the Appeal of U.S. Patent Application No. 09/598,441

Claims of record:

1-33. (Canceled).

34. (Previously presented) An isolated nucleic acid molecule that hybridizes to the nucleic acid depicted in SEQ I D NO:1 in 50% formamide and 6XSSC, at 42°C and after washing conditions of 60°C, 0.5XSSC, 0.1 % SDS, and encodes an amino acid sequence that is at least 80% identical to amino acids 1-118 of SEQ ID NO:2.

35. (Previously presented) The isolated nucleic acid molecule of claim 34, wherein said amino acid sequence is at least 90% identical to amino acids 1-118 of SEQ ID NO:2.

36. (Previously presented) The isolated nucleic acid molecule of claim 34, encoding an amino acid sequence comprising amino acids 1-118 of SEQ ID NO:2.

37. (Previously presented) An isolated nucleic acid molecule that hybridizes to the nucleic acid depicted in SEQ ID NO:1 in 50% formamide and 6XSSC, at 42°C and after washing conditions of 60°C, 0.5XSSC, 0.1% SDS, wherein said molecule is at least 80% identical to the nucleic acid sequence of SEQ ID NO:1.

38. (Previously presented) The isolated nucleic acid molecule of claim 37, wherein said molecule is at least 90% identical to the nucleic acid sequence of SEQ ID NO:1.

39. (Previously presented) The isolated nucleic acid molecule of claim 38 comprising the nucleic acid sequence of SEQ ID NO:1.

40. (Previously presented) The isolated nucleic acid molecule of claim 37 encoding an amino acid sequence comprising the sequence of SEQ ID NO:2.

41. (Previously presented) A recombinant vector that directs the expression of the nucleic acid molecule of claim 34.

42. (Previously presented) A recombinant vector that directs the expression of the nucleic acid molecule of claim 35.

43. (Previously presented) A recombinant vector that directs the expression of the nucleic acid molecule of claim 36.

44. (Previously presented) A recombinant vector that directs the expression of the nucleic acid molecule of claim 37.

45. (Previously presented) A recombinant vector that directs the expression of the nucleic acid molecule of claim 38.

46. (Previously presented) A recombinant vector that directs the expression of the nucleic acid molecule of claim 39.

47. (Previously presented) A recombinant vector that directs the expression of the nucleic acid molecule of claim 40.

48. (Previously presented) A host cell or its progeny transfected or transduced with the vector of claim 41.

49. (Previously presented) A host cell or its progeny transfected or transduced with the vector of claim 42.

50. (Previously presented) A host cell or its progeny transfected or transduced with the vector of claim 43.

51. (Previously presented) A host cell or its progeny transfected or transduced with the vector of claim 44.

52. (Previously presented) A host cell or its progeny transfected or transduced with the vector of claim 45.

53. (Previously presented) A host cell or its progeny transfected or transduced with the vector of claim 46.

54. (Previously presented) A host cell or its progeny transfected or transduced with the vector of claim 47.

55. (Previously presented) The host cell of claim 48, 49, 50, 51, 52, 53, or 54, wherein the host cell is a bacterial cell.

56. (Previously presented) The host cell of claim 48, 49, 50, 51, 52, 53, or 54, wherein the host cell is a yeast cell.

57. (Previously presented) The host cell of claim 48, 49, 50, 51, 52, 53, or 54, wherein the host cell is a plant cell.

58. (Previously presented) The host cell of claim 48, 49, 50, 51, 52, 53, or 54, wherein the host cell is an animal cell.

59. (Previously presented) A method for the production of TIGIRR polypeptide comprising culturing the host cell of claim 48, 49, 50, 51, 52, 53, or 54 under conditions promoting expression.

60. (Previously presented) The method of claim 59, further comprising recovering the polypeptide from the culture medium.

Claims upon entry of amendment filed April 26, 2005:

1-33. (Canceled).

34. (Previously presented) An isolated nucleic acid molecule that hybridizes to the nucleic acid depicted in SEQ I D NO:1 in 50% formamide and 6XSSC, at 42°C and after washing conditions of 60°C, 0.5XSSC, 0.1 % SDS, and encodes an amino acid sequence that is at least 80% identical to amino acids 1-118 of SEQ ID NO:2.

35. (Previously presented) The isolated nucleic acid molecule of claim 34, wherein said amino acid sequence is at least 90% identical to amino acids 1-118 of SEQ ID NO:2.

36. (Previously presented) The isolated nucleic acid molecule of claim 34, encoding an amino acid sequence comprising amino acids 1-118 of SEQ ID NO:2.

37. (Previously presented) An isolated nucleic acid molecule that hybridizes to the nucleic acid depicted in SEQ ID NO:1 in 50% formamide and 6XSSC, at 42°C and after washing conditions of 60°C, 0.5XSSC, 0.1% SDS, wherein said molecule is at least 80% identical to the nucleic acid sequence of SEQ ID NO:1.

38. (Previously presented) The isolated nucleic acid molecule of claim 37, wherein said molecule is at least 90% identical to the nucleic acid sequence of SEQ ID NO:1.

39. (Previously presented) The isolated nucleic acid molecule of claim 38 comprising the nucleic acid sequence of SEQ ID NO:1.

40. (Previously presented) The isolated nucleic acid molecule of claim 37 encoding an amino acid sequence comprising the sequence of SEQ ID NO:2.

41. (Previously presented) A recombinant vector that directs the expression of the nucleic acid molecule of claim 34.

42. (Previously presented) A recombinant vector that directs the expression of the nucleic acid molecule of claim 35.

43. (Previously presented) A recombinant vector that directs the expression of the nucleic acid molecule of claim 36.

44. (Previously presented) A recombinant vector that directs the expression of the nucleic acid molecule of claim 37.

45. (Previously presented) A recombinant vector that directs the expression of the nucleic acid molecule of claim 38.

46. (Previously presented) A recombinant vector that directs the expression of the nucleic acid molecule of claim 39.

47. (Previously presented) A recombinant vector that directs the expression of the nucleic acid molecule of claim 40.

48. (Previously presented) A host cell or its progeny transfected or transduced with the vector of claim 41.

49. (Previously presented) A host cell or its progeny transfected or transduced with the vector of claim 42.

50. (Previously presented) A host cell or its progeny transfected or transduced with the vector of claim 43.

51. (Previously presented) A host cell or its progeny transfected or transduced with the vector of claim 44.

52. (Previously presented) A host cell or its progeny transfected or transduced with the vector of claim 45.

53. (Previously presented) A host cell or its progeny transfected or transduced with the vector of claim 46.

54. (Previously presented) A host cell or its progeny transfected or transduced with the vector of claim 47.

55. (Previously presented) The host cell of claim 48, 49, 50, 51, 52, 53, or 54, wherein the host cell is a bacterial cell.

56. (Previously presented) The host cell of claim 48, 49, 50, 51, 52, 53, or 54, wherein the host cell is a yeast cell.

57. (Previously presented) The host cell of claim 48, 49, 50, 51, 52, 53, or 54, wherein the host cell is a plant cell.

58. (Previously presented) The host cell of claim 48, 49, 50, 51, 52, 53, or 54, wherein the host cell is an animal cell.

59. (Currently amended) A method for the production of SIGIRR ~~TIGIRR~~ polypeptide comprising culturing the host cell of claim 48, 49, 50, 51, 52, 53, or 54 under conditions promoting expression.

60. (Previously presented) The method of claim 59, further comprising recovering the polypeptide from the culture medium.